

WHAT IS CLAIMED IS:

1. A solvated form of crystalline lamotrigine containing a solvate, wherein the solvate is selected from the group consisting of dimethylformamide, dimethylamine, methanol, ethanol, isopropyl alcohol, tetrahydrofuran, and acetone.
2. A crystalline lamotrigine form B.
3. A crystalline lamotrigine, characterized by an X-ray powder diffraction pattern having peaks at about 10.3, 24.2, 25.0, 26.4 and 32.3 ± 0.2 degrees two-theta.
4. The crystalline lamotrigine according to claim 3, further characterized by an X-ray powder diffraction pattern having other typical peaks at about 13.0, 15.8, 17.2, 18.5, 20.5, 21.1, 21.7, 26.1, 27.7, 29.5 and 30.9 ± 0.2 degrees two-theta.
5. A crystalline lamotrigine, characterized by an X-ray powder diffraction pattern as in Fig. 1.
6. The crystalline lamotrigine form B according to claim 2, wherein the crystalline lamotrigine form B is a monosolvate of dimethylformamide.
7. A crystalline lamotrigine form C.
8. A crystalline lamotrigine, characterized by an X-ray powder diffraction pattern having peaks at about 10.1, 10.5, 17.1, 18.4 and 26.2 ± 0.2 degrees two-theta.
9. The crystalline lamotrigine according to claim 8, further characterized by an X-ray powder diffraction pattern having other typical peaks at about 12.4, 13.1, 13.6, 14.4, 16.3, 21.6, 22.5, 23.1, 24.4, 27.4, 27.8, 28.4, 32.7, 33.6 and 34.6 ± 0.2 degrees two-theta.
10. A crystalline lamotrigine, characterized by an X-ray powder diffraction pattern as

in Fig. 2.

11. The crystalline lamotrigine form C according to claim 7, wherein the crystalline lamotrigine form C is a sesquisolvate of dimethylformamide.
12. A crystalline lamotrigine form D.
13. A crystalline lamotrigine, characterized by an X-ray powder diffraction pattern having peaks at about 14.1, 18.2, 15.9, 20.6 and 30.8 ± 0.2 degrees two-theta.
14. The crystalline lamotrigine, further characterized by an X-ray powder diffraction pattern having other typical peaks at about 13.2, 14.9, 17.2, 18.0, 19.0, 19.5, 22.7, 23.0, 23.5, 26.2, 27.0, 27.8, 28.2, 28.6, 29.0, 29.5, 31.0, 32.9 and 33.8 ± 0.2 degrees two-theta.
15. A crystalline lamotrigine, characterized by an X-ray powder diffraction pattern as in Fig. 3.
16. The crystalline lamotrigine form D according to claim 12, wherein the crystalline lamotrigine form D is a $2/3$ solvate of dimethylformamide.
17. A crystalline lamotrigine form E.
18. A crystalline lamotrigine, characterized by an X-ray powder diffraction pattern having peaks at about 9.5, 11.5, 13.8, 23.2 and 26.7 ± 0.2 degrees two-theta.
19. The crystalline lamotrigine according to claim 18, further characterized by an X-ray powder diffraction pattern having other typical peaks at about 13.0, 14.3, 14.9, 15.7, 17.9, 19.4, 20.9, 24.5, 25.6, 27.3 and 32.2 ± 0.2 degrees two-theta.
20. A crystalline lamotrigine form E, characterized by an X-ray powder diffraction pattern as in Fig. 4.

21. The crystalline lamotrigine form E according to claim 17, wherein the crystalline lamotrigine form E is a 2/3 methanolate.

22. A crystalline lamotrigine form E1.

23. A crystalline lamotrigine, characterized by an X-ray powder diffraction pattern having peaks at about 9.6, 13.8, 15.8, 23.1 and 26.7 ± 0.2 degrees two-theta.

24. The crystalline lamotrigine according to claim 23, further characterized by an X-ray powder diffraction pattern having other typical peaks at about 11.6, 13.0, 14.4, 15.2, 16.2, 17.8, 18.9, 20.1, 21.8, 24.6, 25.6, 26.3, 27.3, 27.7, 28.8, 30.0, 30.7, 31.9, 32.3, 32.7, 34.3 and 35.9 ± 0.2 degrees two-theta.

25. A crystalline lamotrigine, characterized by an X-ray powder diffraction pattern as in Fig. 5.

26. The crystalline lamotrigine form E1 according to claim 22, wherein the crystalline lamotrigine form E1 is a 2/3 ethanolate.

27. A crystalline lamotrigine form F.

28. A crystalline lamotrigine, characterized by an X-ray powder diffraction pattern having peaks at about 17.2, 18.7, 26.5, 27.0 and 28.0 ± 0.2 degrees two-theta.

29. The crystalline lamotrigine according to claim 28, further characterized by an X-ray powder diffraction pattern having other typical peaks at about 9.7, 11.8, 12.7, 13.4, 14.6, 15.4, 20.2, 20.7, 21.3, 21.6, 22.0, 24.6, 25.1, 25.5, 28.2, 29.4, 30.1, and 31.8 ± 0.2 degrees two-theta.

30. A crystalline lamotrigine, characterized by an X-ray powder diffraction pattern as in Fig. 6.

31. The crystalline lamotrigine form F according to claim 27, wherein the crystalline lamotrigine form F is a 1/3 solvate of acetone.
32. A crystalline lamotrigine form H.
- 5 33. A crystalline lamotrigine, characterized by an X-ray powder diffraction pattern having peaks at about 9.6, 10.5, 21.8, 22.2 and 27.5 ± 0.2 degrees two-theta.
- 10 34. The crystalline lamotrigine according to claim 33, further characterized by an X-ray powder diffraction pattern having other peaks at about 12.2, 13.5, 14.7, 15.1, 16.5, 16.7, 17.0, 18.5, 19.5, 20.5, 24.0, 24.6, 25.7, 26.3, 28.4, 28.9, 29.4, 30.5, 31.1, 31.8, 33.3 and 35.1 ± 0.2 degrees two-theta.
- 15 35. A crystalline lamotrigine, characterized by an X-ray powder diffraction pattern as in Fig. 7.
36. The crystalline lamotrigine form H according to claim 32, wherein the crystalline lamotrigine form H is a monosolvate of ethanol.
- 20 37. A crystalline lamotrigine form J.
38. A crystalline lamotrigine, characterized by an X-ray powder diffraction pattern having peaks at about 9.5, 10.0, 20.2 and 26.0 ± 0.2 degrees two-theta.
- 25 39. The crystalline lamotrigine according to claim 38, further characterized by an X-ray powder diffraction pattern having other peaks at about 11.6, 12.4, 13.7, 14.8, 15.9, 16.3, 16.6, 17.3, 18.5, 21.0, 21.3, 24.2, 24.4, 24.7, 25.0, 25.5, 26.4, 26.7, 27.8, 29.2, 30.4 and 35.1 ± 0.2 degrees two-theta.
- 30 40. A crystalline lamotrigine, characterized by an X-ray powder diffraction pattern as in Fig. 8.

41. The crystalline lamotrigine form J according to claim 37, wherein the crystalline lamotrigine form J is a monosolvate of isopropanol.

42. A crystalline lamotrigine form K.

43. A crystalline lamotrigine, characterized by an X-ray powder diffraction pattern having peaks at about 11.2, 12.9, 17.2, 21.5 and 22.3 ± 0.2 degrees two-theta.

44. The crystalline lamotrigine according to claim 43, further characterized by an X-ray powder diffraction pattern having other peaks at about 13.5, 17.8, 18.4, 19.2, 20.4, 24.3, 25.3, 25.9, 26.7, 27.0, 28.0, 28.4, 29.0, 29.6, 30.2, 30.6, 31.4, 32.4, and 34.7 ± 0.2 degrees two-theta.

45. A crystalline lamotrigine, characterized by an X-ray powder diffraction pattern as in Fig. 9.

46. The crystalline lamotrigine form K according to claim 42, wherein the crystalline lamotrigine form K is a solvate of tetrahydrofuran.

47. A crystalline lamotrigine form L.

48. A crystalline lamotrigine form L, characterized by an X-ray powder diffraction pattern having peaks at about 12.9, 14.9, 18.2, 20.5, and 25.8 ± 0.2 degrees two-theta.

49. The crystalline lamotrigine form L according to claim 48, further characterized by an X-ray powder diffraction pattern having other typical peaks at about 8.3, 11.3, 11.7, 12.4, 14.1, 16.7, 17.6, 18.4, 19.0, 20.1, 21.7, 22.6, 23.6, 24.6, 26.3, 26.8, 27.8, 28.4, 28.9, 31.1, 31.9, and 33.3 ± 0.2 degrees two-theta.

50. A crystalline lamotrigine form L, characterized by an X-ray powder diffraction pattern as in Fig.10.

51. The crystalline lamotrigine form L according to claim 47, wherein the crystalline lamotrigine form L is a monosolvate of acetone.

52. A crystalline lamotrigine form M.

53. A crystalline lamotrigine, characterized by an X-ray powder diffraction pattern having peaks at about 10.0, 16.5, 16.8, 25.5, and 27.4 ± 0.2 degrees two-theta.

54. The crystalline lamotrigine according to claim 53, further characterized by an X-ray powder diffraction pattern having other typical peaks at about 9.0, 11.4, 13.0, 13.8, 15.1, 17.4, 17.8, 18.6, 21.1, 21.9, 23.8, 26.5, 27.0, 28.0, 28.6, 29.0, 30.1, 32.1, 33.1, and 33.6 ± 0.2 degrees two-theta.

55. A crystalline lamotrigine, characterized by an X-ray powder diffraction pattern as in Fig. 11.

56. The crystalline lamotrigine form M according to claim 52, wherein the crystalline lamotrigine form M is a solvate of dimethylamine.

57. A crystalline lamotrigine form N.

58. A crystalline lamotrigine, characterized by an X-ray powder diffraction pattern having a peak at about 11.6, 13.4, 15.0, 26.9, and 27.7 ± 0.2 degrees two-theta.

59. The crystalline lamotrigine according to claim 58, further characterized by an X-ray powder diffraction pattern having other typical peaks at about 15.9, 16.5, 19.1, 22.2, 22.4, 23.2, 23.5, 26.7, 28.6, 29.9, 30.1, 30.4, 30.7, 31.4, 31.9, 32.9, 33.3, 34.4, 35.0, and 36.2 ± 0.2 degrees two-theta.

60. A crystalline lamotrigine, characterized by an X-ray powder diffraction pattern as in Fig. 12.

61. The crystalline lamotrigine form N according to claim 57, wherein the crystalline lamotrigine form N is a hydrate.

62. A crystalline lamotrigine form O.

63. A crystalline lamotrigine, characterized by an X-ray powder diffraction pattern having peaks at about 9.5, 13.7, 23.0, 26.7, and 28.7 ± 0.2 degrees two-theta.

64. The crystalline lamotrigine according to claim 63, further characterized by an X-ray powder diffraction pattern having other typical peaks at about 8.5, 11.4, 14.2, 15.7, 18.0, 18.9, 24.2, 25.6, 25.9, 27.7, 30.0, 30.7, 32.6, 34.3, and 34.8 ± 0.2 degrees two-theta.

65. A crystalline lamotrigine, characterized by an X-ray powder diffraction pattern as in Fig.13.

66. The crystalline lamotrigine form O according to claim 62, wherein the crystalline lamotrigine form O is a 2/3 methanolate.

67. A crystalline lamotrigine form P.

68. A crystalline lamotrigine, characterized by an X-ray powder diffraction pattern having peaks at about 16.1, 18.1, 18.7, and 26.0 ± 0.2 degrees two-theta.

69. The crystalline lamotrigine according to claim 68, further characterized by an X-ray powder diffraction pattern having other typical peaks at about 8.4, 9.0, 10.1, 12.1, 13.3, 19.5, 20.4, 21.8, 22.5, 24.0, 24.4, 27.4, and 28.3 ± 0.2 degrees two-theta.

70. A crystalline lamotrigine, characterized by an X-ray powder diffraction pattern as in Fig. 14.

71. The crystalline lamotrigine form P according to claim 67, wherein the crystalline lamotrigine form P is a monosolvate of dimethylformamide.

72. A crystalline lamotrigine form Q.

73. A crystalline lamotrigine, characterized by an X-ray powder diffraction pattern having peaks at about 12.4, 13.8, 14.1, 16.6, 17.4, 17.9, 20.0, 21.0, 23.6, 28.8 and 30.9 ± 0.2 degrees 2-theta.

74. The crystalline lamotrigine according to claim 73, further characterized by an X-ray powder diffraction pattern having other typical peaks at about 9.4, 10.0, 26.7, 27.8, and 28.4 ± 0.2 degrees two-theta.

75. A crystalline lamotrigine, characterized by an X-ray powder diffraction pattern as in Fig. 15.

76. The crystalline lamotrigine form Q according to claim 72, wherein the crystalline lamotrigine form Q is a monosolvate of monoisopropanol.

77. A crystalline lamotrigine form R.

78. A crystalline lamotrigine, characterized by an X-ray powder diffraction pattern having peaks at about 10.9, 12.2, 21.0, 27.3, 28.6, and 32.5 ± 0.2 degrees two-theta.

79. The crystalline lamotrigine according to claim 78, further characterized by an X-ray powder diffraction pattern having other typical peaks at about 9.2, 15.7, 19.0, 23.5, and 25.4 ± 0.2 degrees two-theta.

80. A crystalline lamotrigine, characterized by an X-ray powder diffraction pattern as in Fig. 16.

81. The crystalline lamotrigine form R according to claim 77, wherein the crystalline lamotrigine form R is a monosolvate of methyl-isobutyl-ketone.

82. A crystalline lamotrigine form S.

83. A crystalline lamotrigine, characterized by an X-ray powder diffraction pattern having peaks at about 13.4 and 18.7 ± 0.2 degrees two-theta.

84. The crystalline lamotrigine according to claim 83, further characterized by an X-ray powder diffraction pattern having other typical peaks at about 22.4, 26.0, 27.6, and 31.3 ± 0.2 degrees two-theta.

85. A crystalline lamotrigine, characterized by an X-ray powder diffraction pattern as in Fig.17.

86. The crystalline lamotrigine form S according to claim 82, wherein the crystalline lamotrigine form S is anhydrous.

87. A crystalline lamotrigine form U.

88. A crystalline lamotrigine, characterized by an X-ray powder diffraction pattern having peaks at about 12.4, 19.5, 28.4, and 32.1 ± 0.2 degrees two-theta.

89. The crystalline lamotrigine according to claim 88, further characterized by an X-ray powder diffraction pattern having other typical peaks at about 11.5, 15.9, 17.9, 25.4, 25.8, and 26.6 ± 0.2 degrees two-theta.

90. A crystalline lamotrigine, characterized by an X-ray powder diffraction pattern as in Fig. 18.

91. The crystalline lamotrigine form U according to claim 87, wherein the crystalline lamotrigine Q is a monosolvate of methyl tertiary-butyl ether.

92. A pharmaceutical composition comprising a therapeutically effect amount of a lamotrigine solvated crystal form, wherein the lamotrigine solvated crystal form is selected from the group consisting of lamotrigine forms B, C, D, E, E1, F, H, J, K, L, M, N, O, P, Q, R, S and U.

93. A method for treating a patient suffering from epilepsy by administering a therapeutically effective amounts of a lamotrigine crystal form, wherein the lamotrigine solvated crystal form is selected from the group consisting of lamotrigine forms B, C, D, E, E1, F, H, J, K, L, M, N, O, P, Q, R, S, and U.

94. A method of preparing a lamotrigine form B, comprising the steps of 1) dissolving lamotrigine anhydrous in dimethylformamide at about 70⁰C; 2) precipitating the lamotrigine form B by adding water at about 0⁰C; and 3) filtering the lamotrigine form B.

95. A method of preparing a lamotrigine form C, comprising the steps of 1) dissolving lamotrigine anhydrous in dimethylformamide at about 70⁰C; 2) precipitating the lamotrigine form C by adding chloroform at about 0⁰C; and 3) filtering the lamotrigine form C.

96. A method of preparing a lamotrigine form C, comprising the steps of 1) dissolving lamotrigine anhydrous in dimethylformamide at about 70⁰C; 2) precipitating the lamotrigine form C by adding toluene at about 0⁰C; and 3) filtering the lamotrigine form C.

97. A method of preparing a lamotrigine form C, comprising the steps of 1) dissolving lamotrigine anhydrous in dimethylformamide at about 70⁰C; 2) precipitating the lamotrigine form C by adding acetone at about 0⁰C; and 3) filtering the lamotrigine form C.

98. A method of preparing a lamotrigine form C, comprising the steps of 1) dissolving lamotrigine anhydrous in dimethylformamide to form a solution; 2)

stirring the solution at about 25⁰C for about 24 hours; and 3) filtering the lamotrigine form C.

5 99. A method of preparing a lamotrigine form D, comprising the steps of 1) dissolving lamotrigine anhydrous in dimethylformamide at about 70⁰C; 2) precipitating the lamotrigine form D by adding water; and 3) filtering the lamotrigine form D.

10 100. A method of preparing a lamotrigine form E, comprising the steps of 1) dissolving lamotrigine anhydrous in methanol at about 55⁰C; 2) precipitating the lamotrigine form E by adding toluene at about 0⁰C; and 3) filtering the lamotrigine form E.

15 101. A method of preparing a lamotrigine form E1, comprising the steps of 1) dissolving lamotrigine anhydrous in ethanol at about 0⁰C; 2) precipitating the lamotrigine form E1 by adding toluene at about 55⁰C, and 3) precipitating the lamotrigine form E1.

20 102. A method of preparing a lamotrigine form F, comprising the steps of 1) dissolving lamotrigine anhydrous in acetone at about 70⁰C; 2) precipitating the lamotrigine form F by adding cyclohexane at about 0⁰C; and 3) precipitating the lamotrigine by adding cyclohexane.

25 103. A method of preparing a lamotrigine form H, comprising the steps of 1) dissolving lamotrigine anhydrous in ethanol to form a solution; 2) stirring the solution at about 25⁰C for about 24 hours; and 3) filtering the lamotrigine form H.

30 104. A method of preparing a lamotrigine form H, comprising the steps of 1) dissolving lamotrigine anhydrous in isopropanol to form a solution; 2) heating the solution at about 65⁰C; 3) cooling the solution to about 25⁰C for about 5.5 hours; 4) filtering the solution; and 5) drying the solution at about 50⁰C for about 17

hours at about 10 mmHg.

- 5 105. A method of preparing a lamotrigine form J, comprising the steps of 1) dissolving Lamotrigine anhydrous in isopropanol to form a solution; 2) heating the solution to about 65⁰C; 3) cooling the solution to about 25⁰C for about 5.5 hours; 4) filtering the solution; and 5) drying the solution at about 50⁰C for about 17 hours at about 10 mmHg.
- 10 106. A method of preparing a lamotrigine form K, comprising the steps of 1) dissolving lamotrigine anhydrous in tetrahydrofuran to form a solution; 2) stirring the solution at about 25⁰C for about 24 hours; and 3) filtering the lamotrigine form K.
- 15 107. A method of preparing a lamotrigine form L, comprising the steps of 1) dissolving lamotrigine anhydrous in acetone to form a solution; 2) stirring the solution at about 25⁰C for about 24 hours; 3) concentrating the solution to dryness; 4) adding acetone; and 5) filtering the lamotrigine form L.
- 20 108. A method of preparing a lamotrigine form M, comprising the steps of 1) dissolving lamotrigine anhydrous in dimethylamine to form a solution; 2) stirring the solution at about 25⁰C for about 24 hours; and 3) filtering the lamotrigine form M.
- 25 109. A method of preparing a lamotrigine form N, comprising the steps of 1) dissolving lamotrigine anhydrous in water to form a solution; 2) stirring the solution at about 25⁰C for about 24 hours; and 3) filtering the lamotrigine form N.
- 30 110. A method of preparing a lamotrigine form O, comprising the steps of 1) dissolving lamotrigine anhydrous in methanol to form a solution; 2) heating the solution to at about 65⁰C; 3) cooling the solution to about 25⁰C for about 5.5 hours; 4) filtering the solution; and 5) drying the solution at about 60⁰C for about

17 hours at about 10 mmHg.

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111. A method of preparing a lamotrigine form P, wherein the lamotrigine from P is prepared by heating lamotrigine form C monosolvate at about 80°C for about 1 hour.
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112. A method of preparing a lamotrigine amorphous, wherein the lamotrigine amorphous is produced by heating lamotrigine form J isopropanolate at about 80°C for about 1 hour.
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113. A method of preparing lamotrigine form Q, comprising the steps of 1) dissolving lamotrigine anhydrous in isopropanol to form a solution; 2) heating the solution at about 65°C for about 5 minutes; 3) cooling the solution to room temperature; and 3) filtering the lamotrigine form Q.
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114. A method of preparing lamotrigine form R, comprising the steps of 1) dissolving lamotrigine anhydrous in methyl-isobutyl-ketone to form a solution; 2) heating the solution at about 65°C for about 5 minutes; 3) cooling the solution to room temperature; 4) stirring the solution; and 5) filtering the lamotrigine form R.
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115. A method of preparing lamotrigine form S, comprising the steps of 1) dissolving lamotrigine anhydrous in dimethylcarbinol to form a solution; 2) heating the solution at about 65°C for about 5 minutes; 3) cooling the solution to room temperature; 4) stirring the solution; and 5) filtering the lamotrigine form S.
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116. A method of preparing lamotrigine form U, comprising the steps of 1) dissolving lamotrigine anhydrous in methyl tertiary-butyl ether to form a solution; 2) heating the solution at about 65°C for about 5 minutes; 3) cooling the solution to room temperature; 4) stirring the solution; and 5) filtering the lamotrigine form U.